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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,928	04/26/2001	Philippa Marrack	2879-76	2069

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EXAMINER

EWOLDT, GERALD R

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/844,928	Applicant(s) MARRACK ET AL.	
	Examiner G. R. Ewoldt, Ph.D.	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 19-21, 23-33, 52 and 53 is/are pending in the application.
- 4a) Of the above claim(s) 4-8, 10-13, 19-21, 23-33 and 53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9, 14, 15 and 52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Claims 1-15, 19-21, 23-33, 52, and 53 are pending.
2. Claims 4-8, 10-13, 19-21, 23-33, and 53 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions/species.

Claims 1-3, 9, and 14-15, and 52 read on the elected invention and are being acted upon.

3. Applicant's amendment, remarks, and 1.132 declaration of Yosef Refaeli filed 11/17/05, are acknowledged.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 9, 14-15, and 52, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (1998, IDS) in view of Lenardo (1991, IDS) and Refaeli et al. (1998, IDS).

As set forth previously, Zhang et al. teaches that IL-15 causes the "strong and selective" stimulation of memory T cells *in vivo* (see particularly the Summary).

The reference teaching differs from the claimed invention only in that it does not teach the use of IL-15 in an adjuvant formulation nor the inclusion of an IL-2 antibody in said formulation.

Lenardo teaches that IL-2 is required for the programmed cell death of mature (antigen activated) T cells (see particularly the Abstract). The reference further teaches that cells that escape IL-2 induced apoptosis may become memory cells (page 861).

Refaeli et al. expands on the teachings of Lenardo. The reference confirms that activation-induced cell death (AICD) of T lymphocytes is IL-2 mediated. The reference teaches that IL-2 deficient, or IL-2 receptor deficient, mice are resistant to AICD and develop lymphoproliferative disorders (page 615). The reference teaches that recently activated T cells activated in the presence of IL-2 show increased sensitivity to AICD due to increased expression of Fas ligand (FasL) and the inhibition of the AICD inhibitor FLIP (page 619). The reference concludes that IL-2 is involved in T cell homeostasis, i.e., the cytokine has both growth-promoting and

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apoptotic properties. Critically though, the growth properties can be replaced by other cytokines but the apoptotic properties cannot (page 620).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a vaccine adjuvant comprising IL-15 and an anti-IL-2 antibody, given the combined teachings of Zhang et al., Lenardo, and Refaeli et al. One of ordinary skill in the art at the time of the invention would have been motivated to combine IL-15, to stimulate memory T cell production, as taught by Zhang et al., and anti-IL-2 antibody, to remove IL-2 and reduce T cell AICD, as taught by Lenardo, and Refaeli et al., allowing for the maximal production of memory T cells, thus, producing a vaccine adjuvant for the induction of a superior memory immune response.

Applicant's arguments, filed 11/17/05, have been fully considered but they are not persuasive. Applicant again argues that Zhang et al. teaches away from the inhibition of IL-2.

It remains the Examiner's position that the reference teaches that at most, IL-2 has a minimal effect on the production of memory T cells; in most cases IL-2's effect is insignificant, accordingly, it is the Examiner's position that the reference is essentially neutral on the inhibition of IL-2 in memory T cell production.

Applicant argues, "the only motivation to combine the references as the Examiner has done should be found in Lenardo and/or in Refaeli et al."

Applicant is advised that motivation to combine references may also be found "in the knowledge generally available to one of ordinary skill in the art" MPEP 2143.01.

Applicant argues that Lenardo merely speculates that T cells that escape AICD become memory T cells. Accordingly, Applicant argues that the reference is not enabling. Applicant further argues that memory T cells might be refractory to the effects of IL-2, thus, there would be no reason to inhibit IL-2. Finally, Applicant argues, "Lenardo does not speculate that T cells that otherwise undergo apoptosis in the presence of IL-2 may go on to become memory T cells if IL-2 is inhibited; this is rather the Examiner's apparent extrapolation of the statement in Lenardo".

The reference teaches that T cells that escape cell death may become memory cells. It is unclear where Applicant finds the refractory idea in the reference. It is clear, however, that cells that do not escape cell death cannot become memory cells. Accordingly, it remains the Examiner's position that the

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ordinarily skilled artisan would be motivated to provide an agent for the decrease of IL-2 activity to the vaccine of the instant claims.

Applicant argues that Refaeli et al. does not evaluate nor discuss memory T cells. Applicant argues that the reference provides no evidence that protection of mature T cells from AICD will enhance memory T cells.

As set forth above, the reference confirms that activation-induced cell death (AICD) of T lymphocytes is IL-2 mediated. Zhang et al. teaches that memory T cells are "chronically" activated. Accordingly, it remains the Examiner's position that the ordinarily skilled artisan would be motivated to protect memory T cells from AICD by providing an agent for the decrease of IL-2 activity to the vaccine of the instant claims.

Applicant cites a newly submitted 1.132 declaration of Yosef Refaeli. In the declaration Dr. Refaeli states "Although I agree that Lenardo's publication and my own publication (Refaeli et al.) teach that IL-2 enhances AICD of mature, activated T lymphocytes, it is my opinion that one of skill in the art can not say, based on the teachings of either Lenardo or Refaeli et al., that T cells that are affected by AICD are related to memory T cells. Therefore, one also cannot assume, based on these publications, that if mature T lymphocytes are protected from AICD, they will become memory T cells... Accordingly, it does not appear to me to be obvious that inhibition of IL-2 will stimulate memory T cells."

As set forth above, Zhang et al. teaches that memory T cells are "chronically" activated. The Examiner has never put forth the argument that all mature T lymphocytes become memory T cells, it is clear, however, that if the cells are dead, i.e., killed by AICD, they cannot become memory cells. Regarding the obviousness of the instant invention, the Declarant's opinion is noted, however, it carries little weight and is not persuasive.

Applicant again argues the relevance of antigen to the claimed vaccine. Applicant argues that the T cells investigated by Lenardo are not memory cells.

Applicant is advised that the exclusion of antigen from the vaccine of the instant invention comprises an unclaimed limitation. Should Applicant amend the claims to recite a

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vaccine excluding antigen the instant arguments would become more relevant. Applicant's argument that the T cells investigated by Lenardo are not memory cells is noted. The reference goes on to teach that the cells of the reference might become memory cells, thus, it remains the Examiner's position that the ordinarily skilled artisan would be motivated to protect the cells from AICD.

Applicant argues surprising and unexpected results.

Applicant is advised that an assertion of unexpected results comprise a secondary issue. In making such an assertion Applicant is admitting that the invention is obvious, however, patentability lies in the unexpected result. Given Applicant's arguments, this does not appear to be Applicant's position. Additionally, Applicant is advised that the unexpected results must be disclosed in the specification and not first asserted in post-filing arguments.

6. No claim is allowed.


7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

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9. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


2/5/09

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